

Minutes and Actions for Biologics Subteam Discussion (August 21, 2008)

Attendees:

Lydia Falk, Vada Perkins, Dottie Zur-Nedden, Amy Soslow, Theresa Scotchlas, Mary Beth Wilusz, Melita Glavin, Tom Cantu, Terry Brunone, **Note:** If I've left your name off the attendees' list, please let me know.

Minutes:

Hierarchy Worksheets – What's Next

- The Vaccine Hierarchy is now transitioning to the [SRS User Guide](#) as a chapter.
- A Hierarchy Worksheet for the Immune Globulins is in progress at CBER. The Biologics subteam has the opportunity to review this worksheet when available.
- A Hierarchy Worksheet for the Allergenic Extracts is under development at CBER. Review teams at the FDA are currently testing the hierarchy.
- Reminder on the Plasma Derivatives active ingredients. Initial examination of SRS (http://www.fda.gov/oc/datacouncil/1_11_2007SRS_Users_Guide_5B.pdf) Chapter 26: Proteins and Peptides showed inclusion of a majority of the relevant characteristics/tags for plasma derivative active ingredients already.

SPL Stylesheet – Inclusion of AE Reporting contact information

The current stylesheet does not automatically display the VAERS contact information for vaccines. The FDA is working on a solution. Labeling in SPL format will not be placed on DailyMed until the solution is in-place.

Controlled Terminology for Vaccines

- If you find that a Potency Unit seems not to be available for your product, send a request that the term(s) be added to spl@fda.hhs.gov. Include a Reference Standard to aid in documenting the potential Potency Unit.
- UNII Code Assignment: Already Approved products
 - CBER has analyzed existing labeling and assigned UNII codes for active ingredients in current vaccine labels. The analysis is based on a hierarchy of characteristics. Letters containing the *Preferred Name* of each active ingredient,

active moiety, the SRS description from which the *Preferred Name* was derived, and the UNII code are scheduled for delivery to sponsor contacts sometime in the next month (September 2008).

- The *Preferred Name* may not be identical to the free text wording of the active ingredient in the Content of Labeling. Rather, the *Preferred Name* represents the active ingredient in a controlled vocabulary. Sponsors can continue to use their active ingredient wording in the free text.
 - Some manufacturer's ingredients will be similar enough that more than one manufacturer may have the same UNII code.
 - If a Sponsor identifies an error in the description of the active ingredient, they may submit a Level 2 STN response asking for a re-assessment.
 - Requests for UNII codes for legacy (already approved) products should also be sent to spl@fda.hhs.gov.
- UNII Code Assignment: New products
 - *Analysis and identification of UNII codes is now part of the BLA review process.*
 - *Sponsors can include review aids to facilitate the reviewer's analysis of the characteristics of the Biologic under review. For instance, a table containing the identifying characteristics as noted in the SRS would reduce the time needed for a reviewer to extract each of the characteristics from the relevant submission component. This review aid is not required, but may be helpful. This information may also be included in a cover letter, as appropriate.*
 - *Allow several months for assignment of a new UNII code for a new Biologics active ingredient.*
 - *Opportunities for discussion of UNII codes: IND stage - you could capture the UNII code. Bring the question to the reviewers even this early, giving a 3-6 months window before labeling SPL will be submitted. Include as part of a pre-BLA meeting as appropriate. One of the criteria for completion of the review and release of final labeling will be UNII code assignment. Without them, the SPL will be delayed in reaching the DailyMed site.*
 - Inclusion of [ISBT-128](#) codes in Drug Listings. For licensed minimally manipulated cells [currently under Office of Cell and Gene Therapy] covered under CFR 207, ISBT-128 codes can be placed in the NDC Code field.

Submission of SPL Content of Labeling

- SPL must be submitted with relevant CBER applications (BLA, sBLA, CBE, Annual Report) starting October 15, 2008.
- For the first 12 months of CBER content-of-labeling SPL submission: include SPL with Annual Report – even if there have not been changes. This will result in all relevant products having SPL on file at the FDA within one year after implementation. Consult your Reviewer if there may be a delay in submitting an SPL.
- Draft SPL will be reviewed whether or not it has all UNII codes. If the codes are available, fill them in, as this facilitates the review process.
- Final SPL will not pass validation without UNII codes. It will not be posted on the DailyMed site without them.
- For eCTD submissions, SPL is placed in Module 1, section 14 (Labeling) in Draft Labeling or Final Labeling as appropriate. If review aids such as the Vaccine Hierarchy worksheet or equivalent are included, place them in Module 1 as well.
- For other electronic submissions, make sure that the SPL content of labeling files are in their own \SPL folder. This folder must contain the *.xml file and any accompanying figures.
- Drug Listing and Establishment Registration SPL is required starting June 1, 2009. Prior to that, sponsors are being encouraged to submit these SPL through the Voluntary Pilot Program.

Actions:

All Sponsor Reps:

If you are submitting SPL with upcoming CBER submissions for approved products, and need UNII codes for your ingredients, forward the request to spl@fda.hhs.gov and cc: vada.perkins@fda.hhs.gov. Remember that vaccine UNII assignments will be provided to sponsors next month in a formal letter.

If you are submitting SPL with upcoming CBER submissions for new, not-yet-approved products, and need UNII codes for your ingredients, alert the Review Division that UNII assignments are needed for one or more active ingredients and moieties. To facilitate the assignment of UNII codes, you may want to create a document containing the characteristics for your active ingredient(s). This document then would be included in your submission and/or cover letter as an aid to Reviewers.

If you have a content issue for SPL for a particular CBER product (or one that you think crosses products), let Vada know via e-mail (vada.perkins@fda.hhs.gov). He'll raise these issues at the CBER Labeling Subcommittee.

Sponsor Reps with Plasma Derivative products:

Take a look at Chapter 26 of the SRS and see if your product(s)' active ingredient(s) are covered sufficiently by this chapter:

http://www.fda.gov/oc/datacouncil/1_11_2007SRS_Users_Guide_5B.pdf

[Chapter 26 starts on pg 51 (actually pg 56 in the PDF)].

Next Meeting: September 25, 2008 .